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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/888,304

06/22/2001

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09/12/2008

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EXAMINER

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ART UNIT

PAPER NUMBER

1633

MAIL DATE

DELIVERY MODE

09/12/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

Applicant's amendment and response received on 4/28/08 has been entered. Claims 1-26 are pending in the instant application. This application contains claims 14-20 drawn to an invention nonelected with traverse in the reply filed on 5/7/07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 1-13 and 21-26 are currently under examination. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 4/28/08 is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the information disclosure statement has been considered by the examiner and an initialed copy of the 1449 is attached to this action.

Claim Rejections - 35 USC § 103

The rejection of claims 1-12, and 21-26 under 35 U.S.C. 103(a) as being unpatentable over WO 96/04932 (1996), hereafter referred to as Balasubramanian et al., in view of WO 97/25072 (1997), hereafter referred to as Engler et al., is maintained over claims 1-12 and 21-26

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and newly applied to amended claim 13. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant argues that Balasubramanian et al. teaches formulations comprising nonionic surfactants, not cationic surfactants, and that Engler et al. teaches away from combining a cationic surfactant with a high molecular weight block copolymer such as CRL-1005 by showing that neither benzalkonium chloride nor cetylpyridium enhanced gene transfer.

In response, it is noted that Engler was cited to supplement Balasubramanian et al. by teaching that cationic detergents, a class of surfactants, can enhance the delivery of nucleic acids to cells (Engler et al., pages 4-5, and 20-21). In the working examples on pages 14-15, Engler et al. demonstrates that while some surfactants improve gene transfer more than others, Engler et al. clearly shows positive gene transfer using DNA in the form of recombinant adenoviral vector and the cationic surfactants benzalkonium chloride and cetylpyridium. Engler et al. makes the statement that while certain anionic and nonionic detergents enhance gene transfer "dramatically", other cationic and nonionic detergents "did not have similar effects" (Engler et al., page 14). This statement does not imply that such cationic detergents had no effect on gene transfer, just that the effects were not as significant as those observed with other detergents. Engler et al. clearly teaches in other portions of the specification that cationic detergents/surfactants can be used to enhance gene delivery. As such, applicant's argument that Engler et al. teaches away from using cationic detergents is not found persuasive.

Further, it is noted that the instant claims are product claims, not methods claim for using the product to enhance gene delivery or improve expression of a transgene. The claimed product

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elements are obviated by the combined teachings of Balasubramanian et al., who teaches the combination of polynucleotide vaccines, a nonionic surfactant, and an adjuvant comprising a high molecular weight nonionic polyoxyethylene/ polyoxypropylene block copolymers of the general formula $\text{HO}(\text{C}_2\text{H}_4\text{O})_a(\text{C}_3\text{H}_6\text{O})_b(\text{C}_2\text{H}_4\text{O})_a\text{H}$, such as CRL-1005, and Engler et al. who teaches the addition of cationic surfactants to DNA delivery systems in order to improve gene transfer. Further, based on the demonstration by Engler et al. that a formulation comprising a recombinant adenoviral vector and a cationic surfactant such as benzalkonium chloride (BAK) or cetylpyridium can be delivered to cells resulting in detectable gene expression, the skilled artisan would have predicted that a combination as claimed, comprising an adjuvant comprising a high molecular weight nonionic polyoxyethylene/ polyoxypropylene block copolymers of the general formula $\text{HO}(\text{C}_2\text{H}_4\text{O})_a(\text{C}_3\text{H}_6\text{O})_b(\text{C}_2\text{H}_4\text{O})_a\text{H}$, such as CRL-1005, a polynucleotide DNA vaccine, a nonionic surfactant, and a cationic surfactant would be equally capable of being delivered to cells with the result of gene expression.

In regards to newly amended claim 13, the claim now recites specific formulations of the vaccine products selected from a group consisting of 5 mg/mL DNA, 7.5 mg/mL CRL-1005, 0.45 mM BAK in PBS; 5 mg/mL DNA, 7.5 mg/mL CRL-1005, 0.60 mM BAK in PBS; and 5 mg/mL DNA, 7.5 mg/mL CRL-1005, 0.75 mM BAK in PBS. While none of these three specific formulations is specifically taught by either Balasubramanian et al. or Engler et al., Balasubramanian et al. teaches the testing of various formulations of polynucleotide vaccines and CRL-1005 by titrating the amount of vaccine and/or CRL-1005 to determine the best ratio of elements in the formulation for achieving a desired effect, which in the case of Balasubramanian et al. was induction of antibody responses to the encoded antigen (Balasubramanian et al., pages

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8-9, and Figures 5-7). Further, such optimization of the concentrations of elements in a composition for pharmaceutical use was well-known and commonly practiced at the time of filing. As such, it would have been *prima facie* obvious to the skilled artisan at the time of filing to test various formulations of polynucleotide vaccines comprising a DNA polynucleotide vaccine, CRL-1005, and a cationic surfactant such as BAK, including the specific formulations set forth in claim 13 with a reasonable expectation of creating such a formulation and using it to transfect/transduce cells.

Claim Rejections - 35 USC § 112

The rejection of claims 3-4 and 23-24 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of the deletion of the word “between” in these claims.

The rejection of claim 13 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of applicant's amendment which clarifies the elements of the formulations claimed.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

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Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633